HORMONE AND ENZYME DISORDERS

Congenital Hypothyroidism

Congenital hypothyroidism occurs when the thyroid gland fails to produce thyroxine (T4), a hormone necessary for proper central nervous system development. Deficiency of thyroid hormone in an infant usually results in mental retardation and poor growth. The most common causes are total or partial failure of the gland to develop (aplasia or hypoplasia) or development of the gland in an abnormal place (ectopic gland).

Inheritance:	Most cases of congenital hypothyroidism are not genetic
Estimated Incidence:	1:4000
Abnormal Screen Result:	Low T4 and/or Elevated thyroid stimulating hormone (TSH)
Method of Notification:	All results where the TSH is $\geq$ 50 µIU/mL called to physician of record regardless of the T4 level. Any other combinations of results are mailed to physician of record.
Next Steps if Abnormal:	Repeat T4/TSH as soon as possible on filter paper. Consider serum thyroid function tests and referral to pediatric endocrinologist is TSH is very elevated on first specimen. If T4/TSH is still abnormal on repeat filter paper testing, refer to pediatric endocrinologist for further evaluation.
Neonatal Presentation:	None
Treatment:	Thyroxine replacement medication

Special Considerations

Specimen Collection in the First 24 Hours of Life—Interpretation of TSH results is more difficult if the specimen is collected within the first 24 hours of life. This is due in part to the physiologic surge in TSH shortly after birth.

Premature Infants—In some premature infants there appears to be a physiologic reduction in blood T4 levels and occasional elevated TSH levels at birth. These effects are usually transient but these infants need to be closely monitored to ensure that T4/TSH levels achieve normal range as the infants mature.

Formula type—Infants diagnosed with congenital hypothyroidism should not be routinely fed soy based infant formula. It is thought that soy binds with thyroxine replacement medication and slows its absorption.

Later Developing Hypothyroidism—The vast majority of infants with hypothyroidism are detected on the first specimen even if it is collected within the first 24 hours of life. However, in a few cases hypothyroidism develops in the weeks after the initial screening test would have been collected.

Physicians must remain alert to clinical signs of hypothyroidism in older infants despite normal initial screening results.

Congenital Adrenal Hyperplasia (CAH)

Congenital adrenal hyperplasia (CAH) is an enzyme defect which affects the functioning of the adrenal cortex. A metabolic block produces varying degrees of insufficiency of corticosteroids (cortisone and aldosterone) and an excess of male sex hormones. Females have ambiguous or male-like genitalia and will undergo increasing masculinization if untreated. Infants with the salt-losing form of the disorder can develop an acute crisis with failure to thrive, dehydration and shock in the first month of life. Untreated males may present with precocious puberty at 3 to 5 years of age, and untreated females may be virilized. Androgenic compounds also cause accelerated early growth with premature fusion of the epiphyses and ultimate short stature.

Inheritance:	Autosomal recessive
Estimated Incidence:	1:16,000
Abnormal Screen Result:	Elevated 17-OH progesterone
Method of Notification:	All results where the 17-OH progesterone is $\geq$ 100 ng/mL in infants with birth weights $\geq$ 2500 g are called to physician of record. All results where the 17-OH progesterone is $\geq$ 200 ng/mL in infants with birth weights < 2500 g are called to the physician of record. Any other abnormal 17-OH progesterone results are mailed to physician of record.
Next Steps if Abnormal:	**Potential medical emergency.** See infant as soon as possible to ascertain health status. Consult pediatric endocrinologist for further instructions. Repeat 17-OH progesterone as soon as possible on filter paper. Initiate treatment and diagnostic evaluation as recommended by specialist.
Neonatal Presentation:	Females may have ambiguous genitalia.
Treatment:	Replacement of the deficient hormones. If the infant does not have the salt-losing form of CAH, only glucocorticoid (cortisone) is required. For infants with the salt-losing form of CAH, mineralocorticoid (aldosterone) is required in addition to cortisone. Increased dosages of medications are usually required in times of stress, trauma, illness or surgery.

Special Considerations

Specimen Collection in the First 24 Hours of Life—Interpretation of 17-OH progesterone results is more difficult if the specimen is collected within the first 24 hours of life. This is due in part to the physiologic surge in 17-OH progesterone shortly after birth.

Premature/Sick Infants—A large percentage (relative to the overall birth population) of infants with abnormal 17-OH progesterone results are premature and/or sick infants. This is a physiologic response to the stress of prematurity and illness.

Biotinidase Deficiency

Biotinidase is a key enzyme in the biotin cycle. Biotinidase releases biotin from dietary proteins and recycles biotin. Free biotin is necessary for activation of four carboxylase enzymes. Carboxylases are important enzymes in the metabolism of amino acids, in gluconeogenesis, and in the synthesis of fatty acids. Infants who have untreated biotinidase deficiency may develop hypotonia, seizures, developmental delay, ataxia, breathing problems, hair loss and hearing loss.

Inheritance:	Autosomal recessive
Estimated Inheritance:	1:60,000
Abnormal Screen Result:	Deficient Biotinidase
Method of Notification:	All abnormal test results called to physician of record
Next Steps if Abnormal:	Repeat biotinidase as soon as possible on filter paper. See infant as soon as possible to ascertain health status. If biotinidase is still deficient on repeat testing, consult pediatric metabolic specialist for further instructions. Initiate treatment and diagnostic evaluation as recommended by specialist.
Neonatal Presentation:	Usually none. However, some affected infants has presented as early as one week of age.
Treatment:	Daily biotin supplements for life.